Remarks

Upon entry of the amendments submitted herein, claims 23-82 will be pending. Claims 1-22 have been canceled previously or herein without prejudice or disclaimer. Applicants reserve the right to pursue subject matter encompassed by all canceled claims in one or more continuing applications. No new matter has been added.

Rejection of claims 23-36, 40-53, 57-66, and 70-79 under 35 U.S.C. § 101

The rejection of claims 23-36, 40-53, 57-66, and 70-79 under 35 U.S.C. § 101 as allegedly not being supported by either a specific and substantial utility or a well established utility was maintained. *See* Paper No. 42005, page 2. In particular, the Examiner maintained the allegation that "the specification fails to provide sufficient objective evidence of any activity for encoded protein" and that "there is no information pertaining to the significance of the percentage homology, e.g. whether there were any conserved motifs that would lead the artisan to accept the protein's function." *See Id.* at 3.

Applicants respectfully disagree and traverse.

In the first Office Action mailed April 21, 2005, the Examiner introduced the currently pending utility rejection alleging that "the specification fails to provide sufficient objective evidence of any activity for encoded protein." *See* Paper No. 92004, page 3, last paragraph. In the first office action response, passages in the specification were explicitly identified where an activity for the FcR-V polypeptides was indeed asserted. Specifically, Applicant's response pointed out that the specification indicates that FcR-V polypeptides are "important in the regulation of the immune and hematopoietic systems and are 'thought to function as an important trigger of complex immune defense responses'" and "are thought to play a dominant role in type II hypersensitivity reactions." *See* Response to first Office Action, page 13, second full paragraph. Furthermore, Applicants also identified specific immune system related disorders disclosed in the specification for which the FcR-V polypeptides would be useful in treating[1].

[1] The specification teaches that the FcR-V polypeptides are useful for the diagnosis or treatment of specific immune system-related disorders, including "immune-complex related inflammatory diseases such as rheumatoid arthritis, systemic lupus erythmatosis, autoimmune hemolytic anemia, thromboctyopenia and IgG- or IgE-mediated inflammation, anaphylaxis, allergy ....." *See, e.g.,* page 60, paragraph 0135.

Applicants provided explicit evidence from the specification in their previous response showing a specific biological role for the FcR-V polypeptides (i.e., regulation of the immune and hematopoietic systems) and correlated this role to a specific group of immune system-related disorders. Thus, the specific, substantial, and credible elements under 35 U.S.C. § 101 were met in that such a correlation between the biological activity and the asserted use in specific disease conditions would be, more likely than not, sufficient to convince one of skill in the art of the usefulness of the FcR-V protein. Therefore, Applicants have provided evidence of a specific, substantial, and credible utility and have clearly met their burden in rebutting the *prima facie* assertion of lack of utility. *See,* M.P.E.P. 2107 (II)(3)(i).

The Examiner also alleged in the first office action response that "there is no information pertaining to the significance of the percentage of homology, e.g. whether there were any conserved motifs that would [have] led the artisan to accept the protein's function." *See*, Paper No. 92004, page 4. In response, Applicants pointed to specific locations in the specification that disclosed and discussed the importance of the conserved domains between FcR-V and the Fc-γ2 receptor, as well as shared conserved domains between the well-established family of FcR receptors. *See,* Response to first Office Action, page 14, first full paragraph. *See also*, specification pages 4 and 5, paragraph 0012; page 19, paragraphs 0038-0039; and Figure 14.

Additionally, Applicants pointed to the reference by Raghavan *et al.*, cited in the specification, which discloses that "receptors for the Fc domain of immunoglobulins play an important role in immune defense" and the "biological responses elicited [by Fc receptors] include antibody-dependent, cell-mediated cytotoxicity, phagocytosis, release of inflammatory mediators, and regulation of lymphocyte proliferation and differentiation. *See Id.* at page 19, paragraph 0039. *See also*, Raghavan *et al.*, abstract (previously submitted as reference AG with the IDS filed August 16, 2004). The Raghavan *et al.* reference provides further support for the asserted utility by providing additional discussion on the importance of the conserved domains of Fc receptors, by discussing the involvement of Fc receptors in immune defense, and by providing evidence that the science related to Fc receptors was well-known at the time of earliest filing of the present application.

Applicants assert that the disclosure of both the conserved Fc receptor domains of the FcR-V polypeptide and the reference by Raghaven *et al.* further support the credibility of the asserted specific, substantial, and well-established utility for the FcR-V polypeptide and the corresponding antibodies of the present invention. More specifically, when presented with the evidence indicating that: 1) Fc receptor involvement in immune defense was well-known; 2) Fc receptors contain hallmark Ig-like conserved domains; and 3) the FcR-V polypeptide of the present application contains all hallmark Ig-like domains of Fc receptors, one of skill in the art would expect that the FcR-V polypeptides, and thus antibodies that bind FcR-V, would be useful in treating and/or diagnosing disorders of the immune system, such as, for example, allergy and inflammation.

Despite the evidence presented by Applicants in response to the first office action and summarized herein above, the Examiner responded by issuing a final utility rejection that is *nearly verbatim* to the utility rejection presented in the first office action. *Compare* Paper No. 92004, page 3, last paragraph to page 5, second full paragraph *and* Paper No. 42005, page 3, first full paragraph to page 5, second full paragraph. Applicants respectfully submit that the response provided by the Examiner is improper. As stated in the M.P.E.P.:

> Office personnel are reminded that they must treat as true a statement of fact made by an applicant in relation to an asserted utility, unless countervailing evidence can be provided that shows that one of ordinary skill in the art would have a legitimate basis to doubt the credibility of such a statement.

Therefore,

> [i]f the applicant responds to the *prima facie* rejection, the Office personnel should review the original disclosure, any evidence relied upon in establishing the prima *facie* showing, any claim amendments, and any new reasoning or evidence provided by the applicant in support of an asserted specific and substantial credible utility. It is essential for Office personnel to recognize, fully consider and respond to each substantive element of any response to a rejection based on lack of utility.

See M.P.E.P. § 2107(II)(D) (emphasis added).

Moreover, the Examiner's response:

> must establish that it is more likely than not that a person of ordinary skill in the art would not consider that any utility asserted by the applicant would be specific and substantial. The prima facie showing must contain the following elements: (i) An explanation that clearly sets forth the reasoning used in concluding that the asserted utility for the claimed invention is not both specific and substantial nor well-established; (ii) Support for factual findings relied upon in reaching this conclusion; and (iii) An evaluation of all relevant evidence of record, including utilities taught in the closest prior art.

See Id. at § 2107(II)(C)(1)(i-iii) (emphasis added).

Given that the presently pending Final Office Action is nearly a verbatim copy of the previous action, it is readily apparent that the Examiner has not responded to "each substantive element" provided in Applicant's rebuttal argument as required by the M.P.E.P.. This is most particularly apparent as it relates to the significance of the conserved domains for FcR-V or the cited Raghaven *et al.* reference, both of which are disclosed in the specification. Most importantly, the Examiner has not provided any explanation, support, or evidence regarding why one of skill in the art would not believe the asserted utility disclosed in the specification when: 1) presented with the knowledge that the FcR-V polypeptide contains all hallmark conserved domains of Fc receptors; 2) given the well-established roles and biological functions of Fc receptors discussed in Raghavan; and 3) provided with information showing that the Fc receptor art was well-known at the time of the earliest filing of the present application.

In addition to the evidence and explanations previously provided, Applicants herein also point out that the specification teaches that FcR-V polypeptides are expressed by activated monocytes, primary dendritic cells, and macrophages. *See, e.g.*, page 13, paragraph 0024. Hence, given the homology of FcR-V to immune system regulatory molecules[2] with the described tissue expression exclusively in cells of the immune system, one of ordinary

[2] FcR-V contains three pairs of the Ig-like domains in its extracellular domain located around the three pairs of cysteine residues located at positions 33 and 81, 139 and 179, and 228 and 279 of SEQ ID NO:10. The Fc-γ2 receptor is thought to be important in modulation of the immune and hematopoietic systems. The homology

skill in the art would immediately appreciate that the presently claimed antibodies would be useful in regulating immune system functions.

To corroborate the asserted utility for the FcR-V polypeptide, Applicants previously submitted the post-filing date publication by Tedla *et al.* Applicants provided a sequence alignment showing that the LIR7 polypeptide sequence and the FcR-V polypeptide were identical at amino acid positions –16 to 449. Furthermore, Applicants pointed out that both the LIR7 and FcR-V amino acid sequences have Ig-like domains characteristic of FcRs in addition to short cytoplasmic domains and positively charged arginine residues within their transmembrane domains that are characteristic of activating LIRs. Finally, Applicants disclosed that LIR7 activates immunological and/or inflammatory responses which are well-known to play important roles in host responses to inflammation, allergic diseases and parasitic infections. From this information, Applicants explained that Tedla *et al.* further corroborates the asserted utility that FcR-V polypeptides, and thus, that one of ordinary skill in the art would expect antibodies that bind FcR-V to be useful in treating and/or diagnosing disorders of the immune system, such as allergy and inflammation.

Nonetheless, the Examiner alleges that "the sequence of LIR-7 has been disclosed by Borges *et al.* not by Tedla *et al.*, and that sequence alignment of the claimed SEQ ID NO:10 does not show 100% identity over the referenced polypeptide." See, Paper No. 42005, page 5 fourth full paragraph. In support of this argument, the Examiner provided the results of a database search from SwissProt_42 database search showing an alignment of 465 amino acids of the FcR-V polypeptide vs. a 482 amino acid sequence.

Applicants respectfully disagree with the Examiner's conclusion. An analysis of the features section of both the SwissProt_42 analysis provided by the Examiner and the NCBI protein sequence database search for Accession No. Q8N149 (submitted herewith as Exhibit A) reveals that the protein sequence provided by the Examiner actually contains a splice variant at amino acid region 419 to 436. Thus, removal of the splice variant yields a 466 amino acid sequence which was identified by Applicants as LIR7 and which is identical to FcR-V at positions –16 to 449 (SEQ ID NO:10).

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between the Fc-γ2 receptor and FcR-V indicates that FcR-V may also be involved in modulation of the immune and hematopoietic systems. *See, e.g.*, pages 19-20, paragraph 0039.

As further evidence that LIR7 is the 466 amino acid sequence previously aligned with FcR-V, Applicants provide herewith the results of a BLAST of the NCBI refseq_human_aa database. The BLAST was performed with the FcR-V polypeptide sequence and the results show 100% alignment over 465 amino acids with the NCBI protein Accession No. NP_006857.1. *See* BLAST results for alignment gi | 5803068 provided herewith as Exhibit B. An NCBI protein sequence database search result for Accession No. NP_006857.1 (submitted herewith as Exhibit C) identifies this 466 amino acid protein as "leukocyte immunogobulin-like receptor 7" (i.e., LIR7) (*See* "Features" section). Furthermore, the search results also list as Reference 2 (residues 1 to 466) the Tedla *et al.* reference referred to by Applicants herein above and in the previous office action response to corroborate the asserted utility for the FcR-V polypeptide. Thus, Applicants maintain their assertion that the Tedla *et al.* reference further corroborates the asserted utility of the present invention.

Furthermore, the Ig-like domains characteristic of the Fc receptors and the short cytoplasmic domains and positively charged arginine residues within the transmembrane domains, which are characteristic of activating LIRs, are identical between FcR-V and LIR7. Given the that these domains were well-known as significant contributors to the FcR protein's biological function and given the well-established involvement of FcR proteins in immune responses, one of skill in the art would more likely than not find the asserted utility of the present invention to be specific, substantial, and credible.

Finally, while the Examiner's concedes that "Tedla et al., further teach that LIR7 may have a possible function in tempering Th2 cell dependent inflammatory response" the Examiner alleges that there "is no recitation of FcR-V polypeptide or possible function of said polypeptide in inflammatory response." *See,* Paper No. 42005, page 5, fourth full paragraph.

Initially, Applicants assert that the FcR-V polypeptides, and thus, antibodies that bind FcR-V, are useful in treating and/or diagnosing disorders of the immune system, such as allergy and inflammation. As pointed out in the response to the first office action, the specification teaches that the FcR-V polypeptides, which are important in the regulation of the immune and hematopoietic systems, are "thought to function as an important trigger of complex immune defense responses including phagocytosis, antibody-dependent cellular

cytotoxicity, and release of inflammatory mediators" and "appear to play a role in an early step in type II hypersensitivity reactions." *See*, specification, page 16, paragraph 0032. Additionally, the specification teaches that the FcR-V polypeptides are useful for the diagnosis and/or treatment of specific immune system-related disorders, including

> immune-complex related inflammatory diseases such as rheumatoid arthritis, systemic lupus erythmatosis, autoimmune hemolytic anemia, thromboctyopenia and IgG- or IgE-mediated inflammation, anaphylaxis, allergy ....."

See, e.g., page 60, paragraph 0135. Therefore, the specification clearly provides sufficient utility for the FcR-V polypeptide in immune system disorders.

In view of the evidence presented in the response to the first office action and summarized herein, Applicants assert that the totality of the record shows that the asserted utility is well-established, specific, substantial, and credible and therefore the rejection under 35 U.S.C. §101 should be withdrawn. Furthermore, the above evidence and explanations clearly show that the claimed invention has at least one or more patentable utilities. Therefore, Applicants respectfully submit that the rejection of claims 23-36, 40-53, 57-66, and 70-79 under 35 U.S.C. §101 has been obviated and respectfully request that the rejection of the claims be reconsidered and withdrawn.

Rejection of claims 23-36, 40-53, 57-66, and 70-79 under 35 U.S.C. § 112, first paragraph

The rejection of claims 23-36, 40-53, 57-66, and 70-79 under 35 U.S.C. § 112, first paragraph, is maintained based on the premise that "since the claimed invention is not supported by either a specific and substantial, asserted utility or a well established utility for the reasons set forth in the rejection under 35 USC § 101 above, one skilled in the art clearly would not know how to use the claimed invention." *See*, Paper No. 42005, page 6, item 8.

Applicants respectfully disagree and traverse.

Applicants respectfully submit that, as explained above, claims 23-36, 40-53, 57-66, and 70-79 are supported by specific, substantial, and/or well-established utilities. Hence, in view of the present application's disclosure and the state of the art as of its earliest filing date, Applicants submit that a person having ordinary skill in the art would certainly know how to use the claimed invention. Accordingly, Applicants respectfully request the rejection of

pending claims 23-36, 40-53, 57-66, and 70-79 under 35 U.S.C. § 112, first paragraph, be reconsidered and withdrawn.

Rejection of Claims 57-66 and 70-79 under 35 U.S.C. § 112, first paragraph

The rejection of claims 57-66 and 70-79 under 35 U.S.C. § 112, first paragraph, is maintained for allegedly "containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention." *See*, Paper No. 42005, page 6-7, item 9.

Applicants respectfully disagree and traverse.

The test for the written description requirement is whether one skilled in the art could reasonably conclude that the inventor has possession of the claimed invention in the specification as filed. *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563, 19 USPQ2d 1111, 1116 (Fed. Cir. 1991); M.P.E.P. § 2163.02, (emphasis added). The Federal Circuit emphasized the well-settled principle of law that "[t]he written description requirement does not require the applicant 'to describe exactly the subject matter claimed, [instead] the description must clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed,'" *Union Oil Company of California v. Atlantic Richfield Company*, 208 F.3d 989, 54 U.S.PQ.2d 1227 (Fed. Cir. 2000). Further, the Federal Circuit has emphasized the importance of what the person of ordinary skill in the art would understand from reading the specification; and not whether the specific embodiments had been explicitly described or exemplified. Indeed, the court noted, "the issue is whether one of skill in the art could derive the claimed ranges from the patent's disclosure." *Union Oil Company of California v. Atlantic Richfield Company*, 208 F.3d at 1001.

Applicants assert that it was well known in the art at the time of the earliest priority date of this application that the term "expressed from a cell" refers to both a cell surface protein as well as a soluble protein. Furthermore, Applicants submit that one of skill in the art, after reading the entire specification and then reviewing claims 57 and 70, would reasonably conclude that Applicants had possession of a FcR-V polypeptide expressed from a cell (i.e., both FcR-V cell surface polypeptides and soluble FcR-V polypeptides).

Initially, the specification describes on page 1, paragraph 0002, that the FcR-V polypeptide is a member of the Fc receptor family. As disclosed in the specification and as known by one of skill in the art, Fc receptors are cell surface molecules, which consist of an extracellular region, a transmembrane region, and a cytoplasmic region. *See,* specification, page 1, paragraph 0004 and page 2, paragraph 0006. With respect to FcR-V, the specification explicitly describes an extracellular region expressed on the surface of the cell as well as an expressed soluble portion of the FcR-V polypeptide. Specifically, the specification describes embodiments of the FcR-V polypeptide that encompass

> the amino acid sequence of the extracellular domain of the FcR-V polypeptide having the amino acid sequence at positions 1-343 in SEQ ID NO:10, or as encoded by the FcR-V cDNA clone contained in ATCC Deposit No. 209100...the amino acid sequence of the transmembrane domain of the FcR-V polypeptide having the amino acid sequence at positions 344-364 in SEQ ID NO:10, or as encoded by the FcR-V cDNA clone contained in ATCC Deposit No. 209100...the amino acid sequence of the intracellular domain of the FcR-V polypeptide having the amino acid sequence at positions 365-498 in SEQ ID NO:10, or as encoded by the FcR-V cDNA clone contained in ATCC Deposit No. 209100...[and] the amino acid sequence of a soluble FcR-V polypeptide comprising the extracellular and intracellular domains, but lacking the transmembrane domain.

See, specification, page 11, paragraph 0017 (emphasis added).

Further, the specification discloses and defines expressed FcR-V polypeptides in the "Treatment" section of the specification. *See* paragraphs 0141 to 0143. The specification discloses that "the extracellular domain of the protein may be released by proteolytic cleavage as a soluble form from the cells which express the...FcR-V polypeptides" and that "disorders of the immune system can be treated by administration of...FcR-V polypeptides (in the form of soluble extracellular domains or cells expressing the complete proteins)." *See Id.* (emphasis added).

Applicants assert that one of skill in the art, enlightened by the specification, would immediately recognize that the FcR-V protein, by having an extracellular and transmembrane region, would be attached to the cell by way of said transmembrane region and expressed on

the surface of the cell by way of said extracellular region. Additionally, a skilled artisan, after reading the disclosure in the specification, would clearly recognize that a FcR-V polypeptide expressed from a cell would also include a soluble form of the polypeptide.

Accordingly, when the description regarding an expressed FcR-V polypeptide is combined with the antibody disclosure in the specification, one of skill in the art would reasonably conclude that Applicants were in possession of an antibody that binds a protein expressed from a cell. With respect to the specific disclosure for antibodies, the specification describes that "cells expressing the FcR-V proteins...can be administered to an animal in order to induce the production of sera containing polyclonal antibodies" and that monoclonal antibodies can be prepared using hybridoma technology involving an "FcR-V protein expressing cell." *See* paragraphs 0122 to 0125. Therefore, the specification clearly shows that Applicants were in possession of an antibody that binds a protein expressed from a cell (i.e., both FcR-V cell surface polypeptides and soluble FcR-V polypeptides) and have satisfied the requirements of 35 U.S.C. §112.

For all of the above reasons, Applicants respectfully assert that the claimed subject matter was sufficiently described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Thus, Applicants respectfully request that the Examiner's rejection of claims 57-66 and 70-79 under 35 U.S.C. § 112, first paragraph be reconsidered and withdrawn.

Conclusion

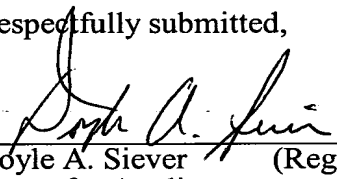
Applicants respectfully request that the above-made remarks be entered and made of record in the file history of the instant application. The Examiner is invited to call the undersigned at the phone number provided below if any further action by Applicant would expedite the examination of this application.

Additionally, Applicants respectfully request to interview with the Examiner in order to more fully discuss the issues and evidence presented previously and herein, if the Examiner concludes that the present application is not in condition for allowance (with other than minor amendments).

Finally, if there are any fees due in connection with the filing of this paper, please charge the fees to our Deposit Account No. 08-3425.

Date: September 20, 2005

Respectfully submitted,



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